Specifically targeting interleukin-13 with tralokinumab improved sleep in two Phase 3, randomised, double-blind, placebo-controlled trials in patients with atopic dermatitis

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Introduction: Sleep loss is common in patients with atopic dermatitis (AD) and contributes to impaired quality of life. Several factors contribute to sleep loss in AD, including pruritus and scratching, skin pain, and dysregulated cytokine levels. Animal and human studies have associated interleukin (IL)-13 injection or increased IL-13 expression with sleep dysfunction. Tralokinumab is a fully human monoclonal antibody that specifically neutralizes IL-13, a key driver of AD signs and symptoms**.** In the pivotal Phase 3 ECZTRA 1 and 2 trials in patients with moderate-to-severe AD, significantly more patients on tralokinumab monotherapy achieved Investigator Global Assessment (IGA) of 0 or 1 (clear or almost clear skin) and 75% improvement in Eczema Area and Severity Index vs placebo at week (week) 16. The objective of this analysis was to determine the effect of tralokinumab monotherapy on sleep loss in moderate-to-severe AD.

Methods: ECZTRA 1 and 2 were duplicate 52-week, randomized, double-blind, placebo-controlled, international trials. Adult patients with AD for ≥1 year who were candidates for systemic therapy were randomized 3:1 to tralokinumab 300 mg or placebo every 2 weeks (q2w) for 16 weeks. Patients recorded by eDiary how much AD interfered with sleep each night using the eczema-related sleep Numeric Rating Scale (NRS). Average sleep loss over the last 3 days/nights was recorded on the previously validated visual analogue scale of SCORing AD (SCORAD) assessed q2w. Patients also scored how many nights they experienced sleep disturbance in the previous week from the previously validated Patient-Oriented Eczema Measure (POEM) assessed q2w.

Results: Eczema-related sleep NRS (weekly average) improved more with tralokinumab compared with placebo in both studies. Change from baseline in eczema-related sleep NRS was larger with tralokinumab vs placebo at each week, with a separation between treatment groups (P<0.001) from week 1. The least-squares mean (LSM) change (standard error [SE]) from baseline at week 16 was greater with tralokinumab vs placebo: –2.6 (0.12) vs –1.9 (0.23); P=0.007 in ECZTRA 1, and –2.9 (0.12) vs –1.5 (0.22); P<0.001 in ECZTRA 2. SCORAD sleep score improved more with tralokinumab vs placebo in both studies. Change from baseline in SCORAD sleep score was greater with tralokinumab vs placebo at each week, with a separation between treatment groups (P<0.01) from week 2. The LSM change (SE) from baseline at week 16 was greater with tralokinumab vs placebo: –2.6 (0.14) vs –1.8 (0.26); P=0.004 in ECZTRA 1, and –3.0 (0.14) vs –1.8 (0.28); P<0.001 in ECZTRA 2. POEM sleep score improved more with tralokinumab vs placebo from week 2 onward (P<0.001), and the LSM change (SE) from baseline to week 16 was greater with tralokinumab vs placebo: –1.2 (0.07) vs –0.6 (0.13) in ECZTRA 1, and –1.3 (0.07) vs –0.6 (0.13) in ECZTRA 2 (both P<0.001).

Conclusions: Tralokinumab monotherapy consistently demonstrated early improvement vs placebo across three measures of sleep in two large Phase 3 trials. Improvement in sleep measures occurred early, at the first postbaseline assessment for each measure. These data highlight that tralokinumab treatment leads to early improvement in sleep loss as early as week 1, consistent with its effects on signs and troublesome symptoms of AD.